Lupkynis™ (voclosporin) – New drug approval

- On January 22, 2021, Aurinia Pharmaceuticals announced the FDA approval of Lupkynis (voclosporin), in combination with a background immunosuppressive therapy regimen, for the treatment of adult patients with active lupus nephritis (LN).
    - The safety and efficacy of Lupkynis have not been established in combination with cyclophosphamide. Use of Lupkynis is not recommended in this situation.
- LN is a potentially serious complication associated with systemic lupus erythematous (SLE). About 200,000 to 300,000 are affected by SLE in the U.S. and approximately one out of three of these individuals have already developed LN at the time of SLE diagnosis. If uncontrolled, LN can lead to permanent and irreversible tissue damage within the kidney, resulting in kidney failure.
- The efficacy of Lupkynis was established in a 52-week, randomized, double-blind, placebo-controlled study in 357 patients with a diagnosis of SLE and with LN. Patients were randomized to receive Lupkynis or placebo, and all patients received background therapy with mycophenolate mofetil and corticosteroids. The primary efficacy endpoint was the proportion of patients achieving complete renal response at week 52. Complete renal response was defined as follows: (1) urine protein to creatinine (UPCR) of ≤ 0.5 mg/mg, and (2) estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73 m^2 or no confirmed decrease from baseline in eGFR of > 20% or no treatment- or disease-related eGFR-associated event at time of assessment.
    - At week 52, complete renal response was achieved in 40.8% vs. 22.5% of patients receiving Lupkynis vs. placebo, respectively (odds ratio: 2.7; 95% CI: 1.6, 4.3; p < 0.001).
- Lupkynis carries a boxed warning for malignancies and serious infections.
- Lupkynis is contraindicated in:
    - Patients concomitantly using strong CYP3A4 inhibitors (eg, ketoconazole, itraconazole, clarithromycin) because these medications can significantly increase exposure to Lupkynis which may increase the risk of acute and/or chronic nephrotoxicity
    - Patients who have had a known serious or severe hypersensitivity reaction to Lupkynis or any of its excipients.
- Additional warnings and precautions for Lupkynis include nephrotoxicity, hypertension, neurotoxicity, hyperkalemia, QTc prolongation, immunizations, and pure red cell aplasia.
- The most common adverse reactions (≥ 3%) with Lupkynis use were decreased glomerular filtration rate, hypertension, diarrhea, headache, anemia, cough, urinary tract infection, abdominal pain upper, dyspepsia, alopecia, renal impairment, abdominal pain, mouth ulceration, fatigue, tremor, acute kidney injury, and decreased appetite.
- The recommended starting dose of Lupkynis is 23.7 mg orally twice a day. The dosage of Lupkynis is based on the patient's eGFR. The dosage should be modified based on eGFR.
    - Lupkynis should be used in combination with mycophenolate mofetil and corticosteroids.
    - Prior to initiation of therapy, an accurate baseline eGFR should be established. Use of Lupkynis is not recommended in patients with a baseline eGFR ≤ 45 mL/min/1.73 m^2 unless the benefit exceeds the risk; these patients may be at increased risk for acute and/or chronic

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nephrotoxicity. In addition, blood pressure should be checked at baseline. Lupkynis should not be initiated in patients with blood pressure > 165/105 mmHg or with hypertensive emergency.
  - If the patient does not experience therapeutic benefit by 24 weeks, discontinuation of Lupkynis should be considered.

- Aurinia Pharmaceuticals plans to launch Lupkynis immediately. Lupkynis will be available as 7.9 mg capsules.